Diabetes Asia Journal
Vol. 1, Issue 2, Oct 2024, Edition: Online
Publisher: Diabetes Asia Journal under JHRC
eISSN: 3048-8192
Cross Ref DOI: 10.62996/daj.30112024
Journal Homepage: https://diabetesasia.org/journal/

Review of TOBOGM Study

Editorial Review: Rajesh Jain

108 B Gandhi gram, Vinobha Nagar, Kanpur-208007, India. Email: drrajeshjain@diabetesasia.org

Simmons D, Immanuel J, Hague WM, Teede H, Nolan CJ, Peek MJ, Flack JR, McLean M, Wong V, Hibbert E, Kautzky-Willer A, Harreiter J, Backman H, Gianatti E, Sweeting A, Mohan V, Enticott J, Cheung NW; TOBOGM Research Group. Treatment of Gestational Diabetes Mellitus Diagnosed Early in Pregnancy. N Engl J Med. 2023 May 5. doi: 10.1056/NEJMoa2214956

In this TOBGM study, Intervention started very late, with OGTT performed an average of 15.6 weeks. And this is why it results in a modest reduction in primary outcome in the immediate treatment arm (24.9% Vs. Control group (30.5%), adjusted risk reduction 5.6%. OGTT was performed in less than 14 weeks in 23.2% of Women only, and most of the women were beyond the 14th week at entry level in both the Intervention and control groups. Insulin and Metformin use was more in the Treatment arm than in the control arm, 58.1% vs. 41.4% and 23.6% Vs. 10.4%, respectively. Interestingly, more benefits were seen in less than the 14th week of pregnancy.
Our theory says that if a Diagnosis could have been made in the 8th week by a Postprandial Blood Glucose value threshold of 110 mg/dl and treatment with MNT and Metformin 250 mg Two times to maintain Postprandial Blood glucose at 2 hours with less than 110 mg/dl would have resulted in a more robust reduction in Neonatal and Maternal outcomes. This theory is based on Dr. V Seshiah's" Path Breaking Concept for Primordial Prevention of Gestational Diabetes and its sequelae. Prof Seshiah is well known Expert on Gestational Diabetes and received the IDF lifetime achievement award and Padmashri from Govt of India for his work in GDM.

Diabetes mellitus in recent years has become a relentlessly evolving pandemic. Measures for the screening and early detection of diabetes are practiced worldwide. However, considering the ever-increasing magnitude of the problem, the current efforts should primarily focus on the primordial prevention of diabetes.

A ray of hope for preventing the development of diabetes in an individual arises from the concept that many adult-onset diseases have already been programmed while the individual is still in-utero. In women with hyperglycemia in pregnancy, maternal hyperglycemia results in fetal hyperinsulinemia, leading to increased fetal adiposity insulin resistance and diabetes in adulthood. We have pointed out that the fetal beta-cells start secreting insulin at 10-11 weeks of pregnancy, and fetal hyperinsulinemia persists with maternal hyperglycemia in a pregnant woman who would develop gestational diabetes.

Considering the fetal glucose-steal phenomenon and the fetal renal threshold for glucose, we have suggested a two-hour post-prandial blood-glucose (PPBG) value of >110 mg/dL as the cut-off for the prediction of gestational diabetes in the early weeks of pregnancy. Furthermore, we have emphasized using metformin in addition to medical nutrition therapy in the early weeks to maintain PPBG around 110 mg/dL to prevent gestational diabetes.

We recommend universal screening of all pregnant women during the early weeks of the first trimester. We put forward that a two-hour PPBG of >110 mg/dl during the 10th-11th week of pregnancy would predict the risk of gestational diabetes in the pregnant woman. We suggest early testing and intervention prevent the development of fetal hyperinsulinemia as a primordial prevention approach for diabetes[1]

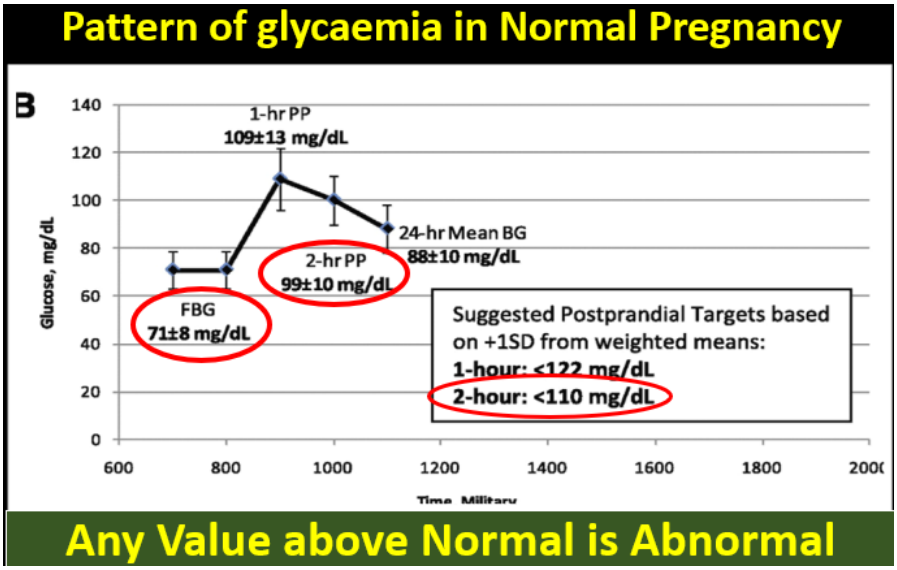

Figure 1. The pattern of glycemia in normal pregnancies and recommended therapeutic targets for post-prandial blood glucose in hyperglycemia-in-pregnancy (HIP). Adapted from Hernandez et al., 2011 [9], under the Creative Commons License http://creativecommons.org/licenses/by-nc-nd/3.0/)

A blood test conducted as early as the 10th week of pregnancy may help identify women at risk for gestational diabetes; if> 110 mg/dl, MNT and metformin 250 mg/bd must be started and continued. The target glycemia to be obtained is PPBS 99 ± 10 mg/dl. Metformin is Safe as the Embryonic stage is over by the 8th week.

[2]To use metformin as an adjunct or alternative to insulin in the preconception period and during pregnancy, when the likely benefit from improved blood glucose control outweighs the potential for harm.

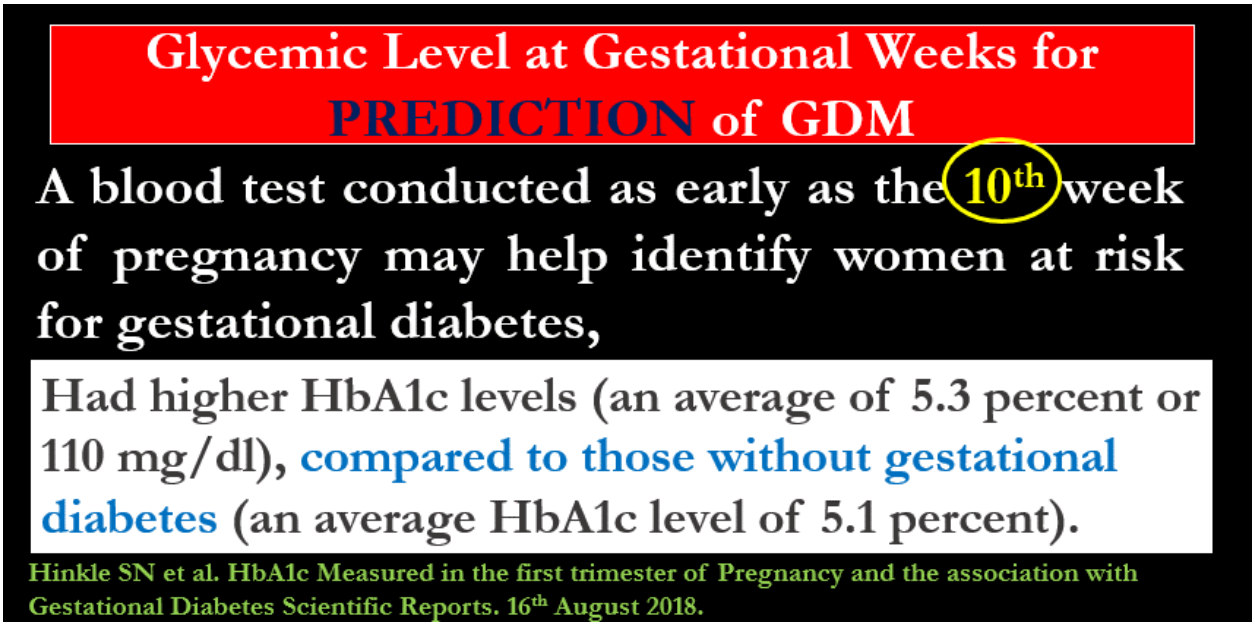
Glycemic Level at Gestational Weeks for PREDICTION of GDM
A blood test conducted as early as the 10th week of pregnancy may help identify women at risk for gestational diabetes,
Had higher HbA1c levels (an average of 5.3 percent or 110 mg/dl), compared to those without gestational diabetes (an average HbA1c level of 5.1 percent).
Hinkle SN et al. HbA1c Measured in the first trimester of Pregnancy and the association with Gestational Diabetes Scientific Reports. 16th August 2018.

Figure 2 Glycemic level at Gestational Weeks for Prediction of GDM

[3]Administration of metformin after the 12th week will not prevent GDM.

PPBS >110 mg/dl at 1oth week Insulin resistance physiologically plays a vital role in the changes in carbohydrate, lipid, and amino acid metabolism that facilitates anabolism and nutrition to the fetus.

The idea is to test for glucose tolerance in the 8th week (2 months). Why? Prediction of GDM is 2hr PPBS > 110mg/dl at 10th week. Hence in the 8th week itself, PPBS has to be estimated. Because…In case PPBS is > 110 mg/dl in the 8th week, a grace period of 2 weeks is available to attain PPBS < 110 mg/dl in the 10th week[4]

The aim is to maintain Maternal 2hr Plasma Glucose 99 ± 10 mg/dl Throughout Pregnancy from Conception to Confinement to Prevent Transgenerational Transmission of Diabetes.

The Preliminary data from India show the benefit of early treatment of GDM as per the RCT being going on in 8 centers in India across different states by DIPSI Diabetes in pregnancy study group India.

1. Seshiah V, Bronson SC, Balaji V, Jain R, Anjalakshi C. Prediction and Prevention of Gestational Diabetes Mellitus and Its Sequelae by Administering Metformin in the Early Weeks of Pregnancy. Cureus. 2022 Nov 15;14(11):e31532. doi: 10.7759/cureus.31532. PMID: 36540507; PMCID: PMC9754731.

2. NICE Guidelines. 2nd February 2015

3. Valdés E, Sepúlveda-Martínez A, Candia P, Abusada N, Orellana R, Manukian B, Cuellar E. Metformin as a prophylactic treatment of gestational diabetes in pregnant patients with pregestational insulin resistance: A randomized study. J Obstet Gynaecol Res. 2018 Jan;44(1):81-86. Doi: 10.1111/jog.13477

4. Hernandez TL, Friedman JE, Van Pelt RE, Barbour LA. Patterns of Glycemia in Normal Pregnancy: Should the current therapeutic targets be challenged? Diabetes Care. 2011 Jul;34(7):1660-8

- **Acknowledgment**

  Not applicable

- **Funding**

  Not applicable

- **Informed Consent**

  Not applicable

- **Conflict of Interest Statement**

  All the authors declared “No Conflict of Interest” with this publication.

The article is Open Access and are licensed under a Creative Commons Attribution 4.0 International License, visit http://creativecommons.org/licenses/by/4.0/

- **DOI:** 10.62996/daj.30112024

- **Cite this Article**

Rajesh Jain.[1]. **Review of TOGOBM study.** Diabetes Asia Journal.2024; 1(2):35-37. https://doi.org/10.62996/daj.30112024